REMARKS

Upon entry of the instant amendment claims 24, 28, 30, 35 to 46, 49 and 50 are pending, of which claims 28 and 36 where withdrawn from consideration by the Examiner. Claim 50 is new and has support in the specification on page 5, lines 15 to 16. Thus, no new matter has been added.

The Office Action dated September 10, 2007 has been carefully reviewed and the following reply is made in response thereto. In view of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants acknowledge that the Rejections under 35 U.S.C. 102 (e) and 35 U.S.C. 103 (a) in view of Schenk *et al.* have been withdrawn.

Election/Restriction

On page 3 of the Office Action, the Examiner has withdrawn claims 28 and 36 from examination at this time as they are directed to antibodies that are generated to light chain amyloid and that cross-react with β-amyloid, and that it is not evident that the opposite is true. Thus, a search for antibodies that opsonize and/or react with non-light chain amyloid is not the same as, nor co-extensive with a search for antibodies generated to light chain amyloids.

Going back to the original species election, Applicants elected the species of "immunoglobulin reactive with a non-light chain amyloid as the functional species" on February 22, 2002. Applicants respectfully submit that the subject matter of claims 28 and 36 is directed to this reactive species, regardless of the source of fibrils from which the antibodies were raised. As discussed in the instant application, antibodies raised against immunoglobulin light chain (claim 28), such as the deposited antibodies of claim 36, react with non-light chain amyloid and are an elected species. For instance, the specification at page 20, lines 7-14, teaches that antibodies raised against immunoglobulin light chain fibrils react against AA-amyloid as well as fibrils made from Aβ protein (both non-light chain amyloid as originally elected). Without being limited to any specific mechanism of action, the specification discloses that, for instance, the deposited monoclonals (those same deposits as set forth in claim 36) recognize an epitope(s) that

"may be a general feature of amyloids." (page 18, lines 17-21, see also Example 6). Thus, Applicants submit that claims 28 and 36 claim "immunoglobulin reactive with a non-light chain amyloid as the functional species" as originally elected. These claims fall within the scope of the elected group. Applicants respectfully request that claims 28 and 36 be rejoined with the elected claims currently under examination.

The rejection of claims 24, 30-31, 35, 39-46 and 48-49 as being anticipated under 35 U.S.C. § 102(b) by Konig *et al.* (WO 96/25435)

Applicants have reviewed the Examiner's restatement of the pending rejection and reasoning concerning the maintenance of this rejection. Applicants submit the Examiner has not met her burden of establishing a *prima facie* case of anticipation. Applicants respectfully submit that a claim is anticipated only if each and every element at set forth in the claim is found in the prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Applicants assert that Konig *et al.* do not teach each and every limitation of the claimed invention.

The Examiner asserts that Konig's disclosure on page 25, lines 14 -18, "[t]hus the monoclonal antibody and methods of the instant invention are useful for diagnostic and therapeutic uses in all immunological and related methodologies which can be applied to the detection, monitoring, extraction, inhibition and modification of the unique βA4 species, in the diagnosis and treatment of AD," teaches use of specific antibodies in methods of treatment for Alzheimer's disease and administration of antibodies in pharmaceutical formulations to Alzheimer's patients. To support her latter point, the Examiner further cited to the following disclosure in Konig: "Thus the instant invention also provides for methods for the prevention of aggregation of βA4 peptide by administering monoclonal antibody of the instant invention." Again, the passages cited do not anticipate all elements of the claimed invention. However, the Examiner argues that the missing element is inherently present and asserts that Applicants have not provided any facts that the antibody of Konig fails to work *via* opsonization and that only assertions are provided. However, by showing that C-terminal antibodies, of which the monoclonal antibody disclosed by Konig 369.2B is a member, Applicants respectfully submit that they have met their burden and provided a fact that the antibody of Konig does not necessarily opsonize and consequently fails to inherently anticipate the presently claimed

invention. Applicants are further confused by the Examiner's request for applicants to show "unobvious difference" between teachings of the prior art reference and Applicants' claims under an anticipation rejection. As admitted by the Examiner, Konig does not disclose a mechanism of action for opsonization, thus one of skill in the art would not have any direction to solve that problem.

In addition, Applicants point out that claims 30 to 33 are directed antibodies that are human, humanized, or chimeric. Konig does not state nor even contemplate that the antibodies disclosed in said reference can be human, humanized or chimeric. Thus, Konig does not anticipate claims 30 to 33. In view of the above arguments, Applicants request that the rejection under 35 U.S.C. 102 (b) be reconsidered and withdrawn.

The rejection of claims 24, 30-35 and 37-49 as being anticipated under 35 U.S.C. § 102(b) by Becker *et al.* (EP 613,007)

Applicants submit the Examiner has not met her burden of establishing a *prima facie* case of anticipation. Applicants assert that Becker *et al.* do not anticipate the claims because Becker *et al.* do not enable a person of skill in the art to use the invention as currently claimed. Applicants further point out that new claim 48 claims a human antibody, which is not disclosed in Becker *et al.*

Applicants respectfully to point out that "[a] claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." *Amgen v. Hoechst Marion Roussel, Inc.* 314 F.3d 1313, 1354 (Fed. Cir. 2003). Also, prior art is not enabling so as to be anticipating if it does not enable a person of ordinary skill in the art to carry the invention. See *Elan Pharms., Inc. v. Mayo Found.*, 346 F.3d 1051, 1057 (Fed. Cir. 2003). A prior art reference is enabled only if "routine experimentation is required in order to practice a claimed invention, but…such experimentation must not be 'undue.'" *Amgen v. Hoechst Marion Roussel, Inc.* 457 F.3d 1293 (Fed Cir. 2006) (quoting Enzo *Biochem, Inc. v. Calgene, Inc. 188 F.3d 1362, 1371* (Fed. Cir. 1999)). When considering whether or not a prior art reference requires "undue experimentation" we look at the reference from the perspective of a person of ordinary skill in the art. *Amgen v. Hoechst Marion Roussel, Inc.* 79 USPQ2d 1705, 1715 (Fed Cir. 2006). The factors relevant in determining whether undue experimentation is

required include: (1) the quantity of experimentation; (2) the amount of direction or guidance present; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability of unpredictability of the art; and (8) breadth of the claims. *Impax v. Aventis*, 496 F. Supp. 2d 428, 432 (D. Del. 2007) (citing *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988))[1].

In the instant case, Becker *et al.* do not anticipate the claims because Becker *et al.* do not enable a person of skill in the art to use the invention. Specifically, Becker *et al.* fail to demonstrate an antibody to administer to a patient to remove amyloid deposits, as required by the claims. The Examiner asserts that because Becker *et al.* states that the antibodies disclosed can be used therapeutically, thus "[o]ne of skill in the art would immediately recognize that such would mean administration of the antibody in an amount sufficient to elicit an effective (i.e. therapeutic) response." Sept. 10, 2007 Office Action, page 10. However, a person of skill in the art after reviewing Becker *et al.* would require performing an undo amount of experimentation to create and select an antibody to administer to a patient to remove amyloid deposits *in vivo*. There is no guidance in Becker *et al.* for one of skill in the art to determine whether it would opsonize the amyloid deposits, as required by the presently claimed invention.

Applying the relevant determining factors of whether undo experimentation is required (*In Re Wands*, as stated above), Becker does not enable a person of skill in the art to determine an effective amount of antibody to be administered to a patient to remove amyloid deposits *in vivo*.

The first factor considered is the quantity of experimentation. As stated in the previous response, dated June 8, 2007, no effective animal model existed that could show that amyloid masses could be removed by an antibody *in vivo*. The instant specification discloses, for the first time, an antibody removing amyloid deposits in an animal model. Thus, after reading Becker, a person of ordinary skill in the art would have to perform an undue amount of experimentation because Becker does not provide guidance or refer to any experiments or models that can be used to determine the effective amount of antibody to administer to a patient to remove amyloid

[1] The factors enumerated in *In re Wands* are normally applied to a prior art document under an obviousness analysis. However, in *Impax v. Aventis*, 496 F. Supp. 2d 428, 432 (D. Del. 2007) the court used the *In re Wands* factors to analyze a 35 U.S.C. 102 (b) reference to determine if said reference was enabled and thus determine if said reference anticipates the patent in question.

deposits *in vivo*. Thus, a person would need to develop their own model and no guidance is given by Becker.

Second, with respect to the amount of direction and guidance that Becker provides, Applicants assert that Becker does not disclose any guidance on how to "therapeutically" administer an antibody for the treatment of Alzheimer's disease, or even to administer an effective amount of antibody to a patient to remove amyloid deposits *in vivo*. Becker does not disclose specific methods or modes of administering antibodies to a patient. Becker does not even contemplate how to determine an effective amount of an antibody to be delivered to remove amyloid deposits *in vivo*. In addition, the term "therapeutic" is not defined in the disclosure. Therapeutic could mean removing amyloid *peptide* from the body (Becker only disclose antibodies that bind to peptides), not necessarily removing amyloid deposits, as required in the instant claims. Thus, the fact that Becker does not provide a model to determine an effective amount antibody to remove amyloid deposits *in vivo*, does not provide specific methods of administration, or even what therapeutic method they are referring to, Applicants assert the there is no guidance in Becker on how to determine the effective amount of antibody to remove amyloid deposits in a patient.

Third, with respect to examples in the reference, there are only *in vitro* examples in Becker, comparing neurotoxicity of β-amyloid *peptide* with and without β-sheet structure. There are no disclosure of any specific antibody, no antibody created, and no experiments with any antibody. Further, there are no *in vivo* data at all. Thus, the examples in this reference cannot help guide a person of skill in the art to determine the effective amount of an antibody to remove amyloid deposits *in vivo* or to create an antibody that removes amyloid deposits at all.

Next, with respect to the state of the prior art, there was no effective animal model in existence that could show that amyloid masses could be remove by an antibody *in vivo*. In addition, to the knowledge of Applicants, no one has ever described antibody mediated amyloid removal *in vivo*, not to mention the *effective amount* of an antibody to be administered to a patient for removing deposits *in vivo*. Thus, there is no guidance on the prior art.

Finally, with respect to predictability in the art, Applicants assert that not all antibodies can opsonize a target. One confirmation of this fact is the Schenk reference, U.S. patent

6,743,427 in which they described the inability of C-terminal antibody 16C11 to remove amyloid deposits.

Thus, in view of the above arguments, Applicants assert the Becker *et al.* do not anticipate the instant claims because Becker *et al.* do not enable a person of skill in the art to determine an antibody to be administered to a patient to remove amyloid deposits *in vivo*. Thus, applicants request that this rejection under 35 U.S.C. 102 (b) be reconsidered and withdrawn.

CONCLUSIONS

Applicants respectfully submit that the pending claims are now in condition for allowance The Examiner is hereby invited to contact the undersigned for any remaining issues.

Respectfully submitted,
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